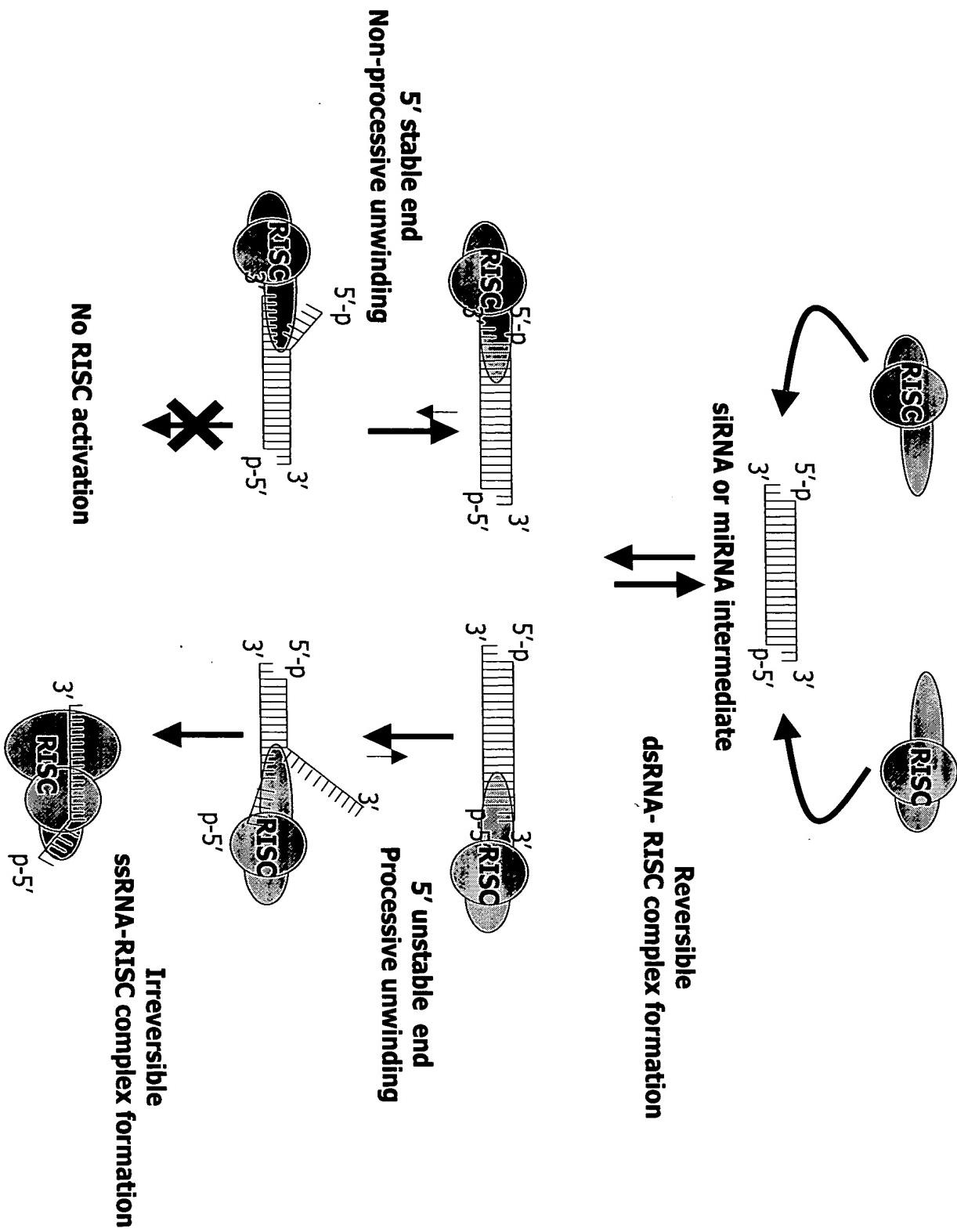


Figure 1



siRNA panel (270)

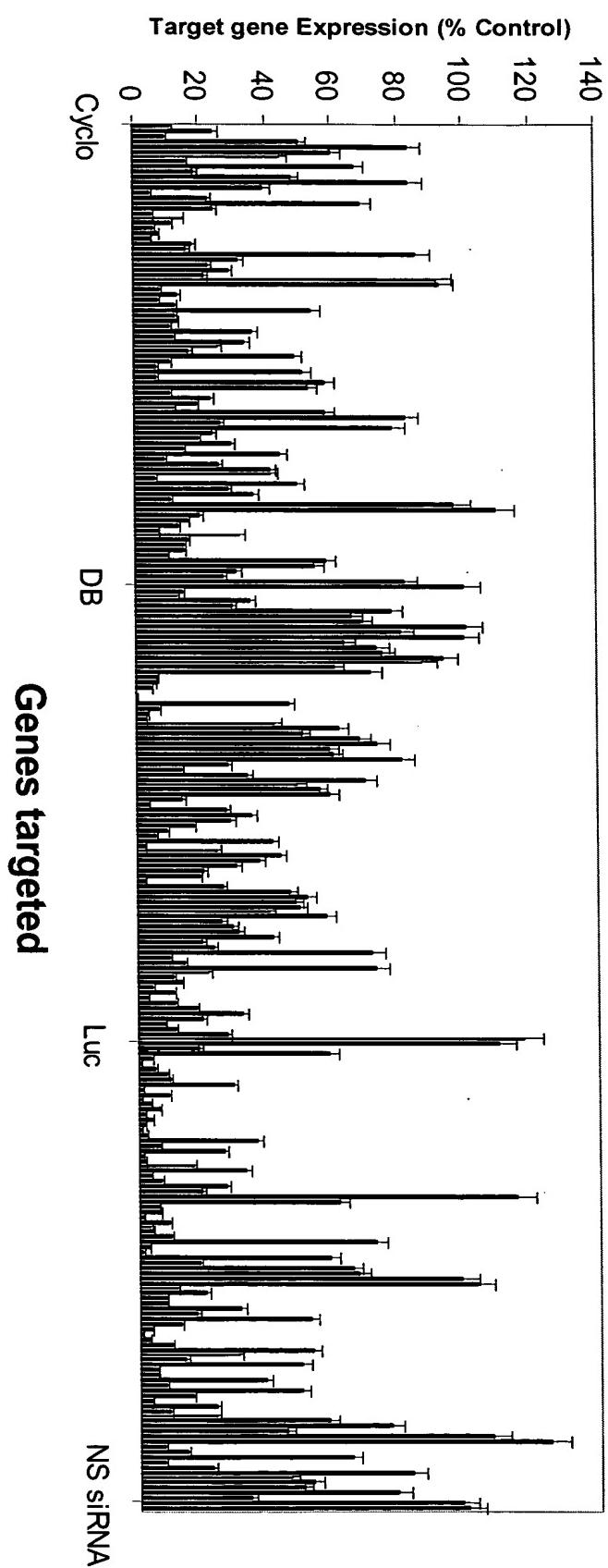


Figure 2

siRNA functionality is independent from the cell line

Figure 3a

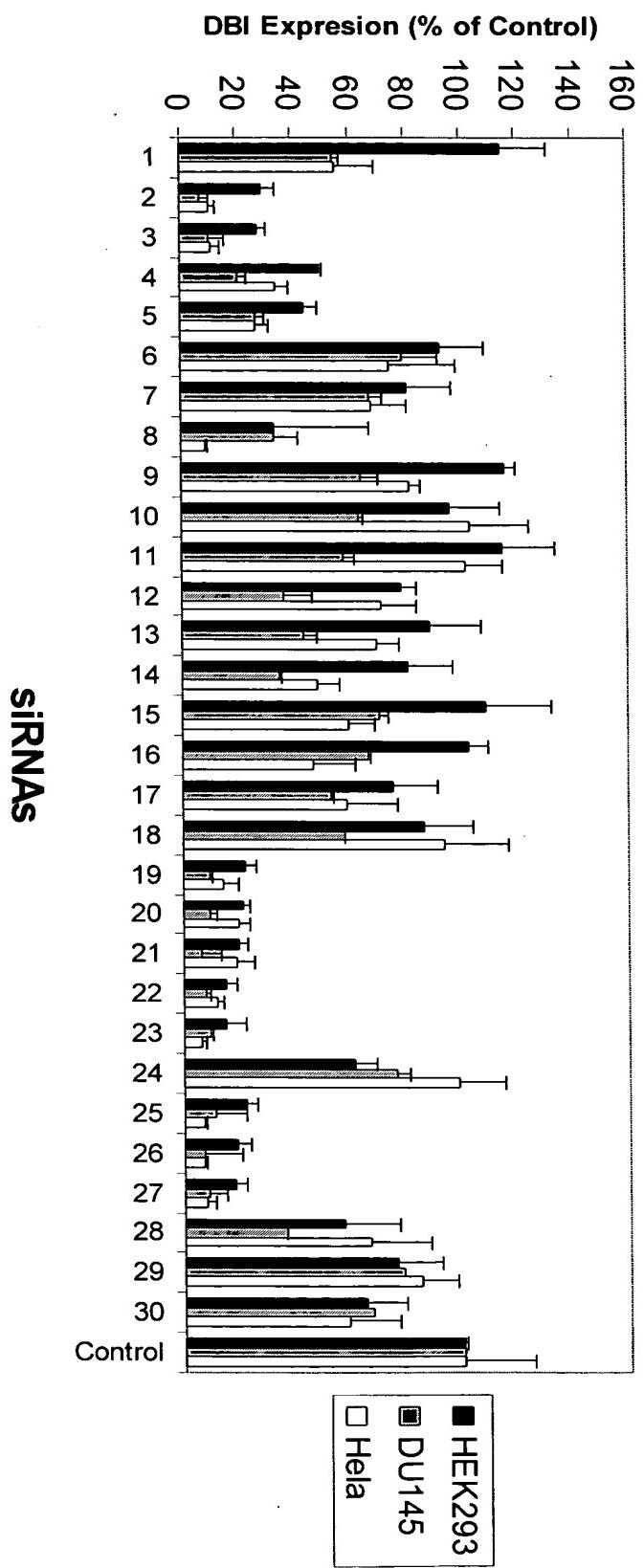


Figure 3b

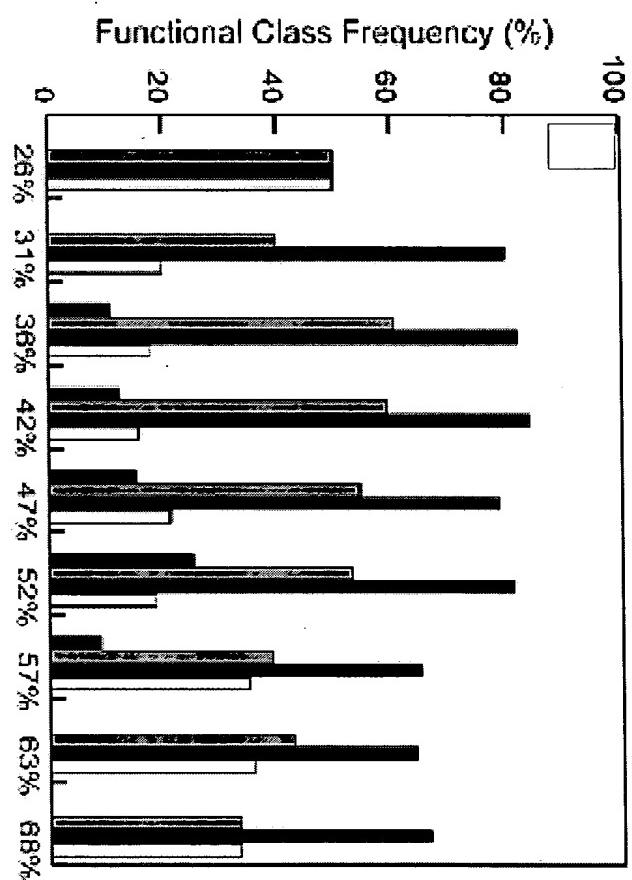


Figure 3c

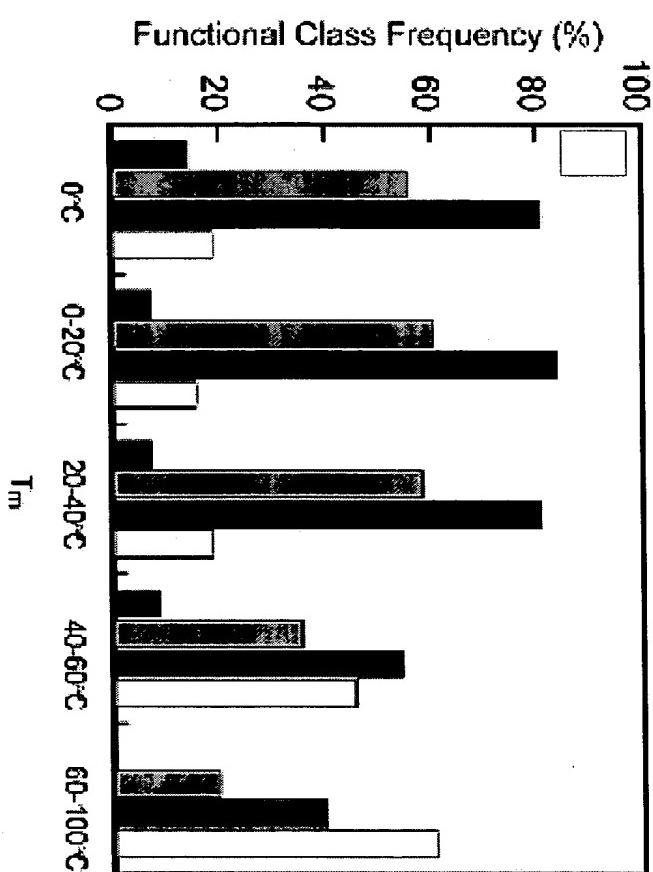


Figure 4

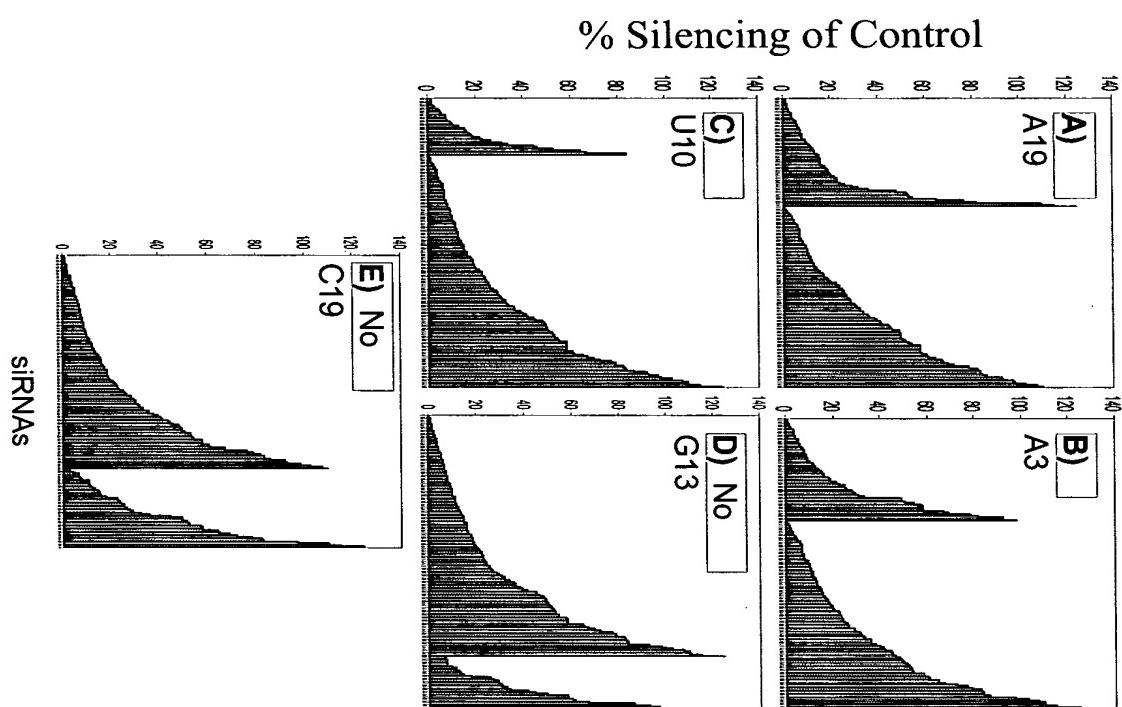


Figure 5A

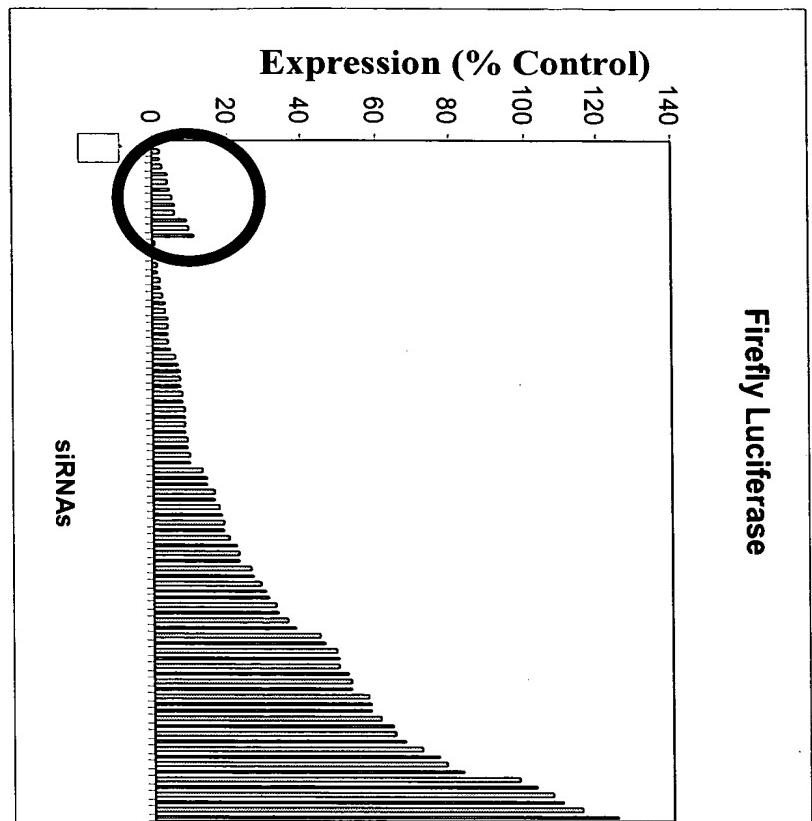
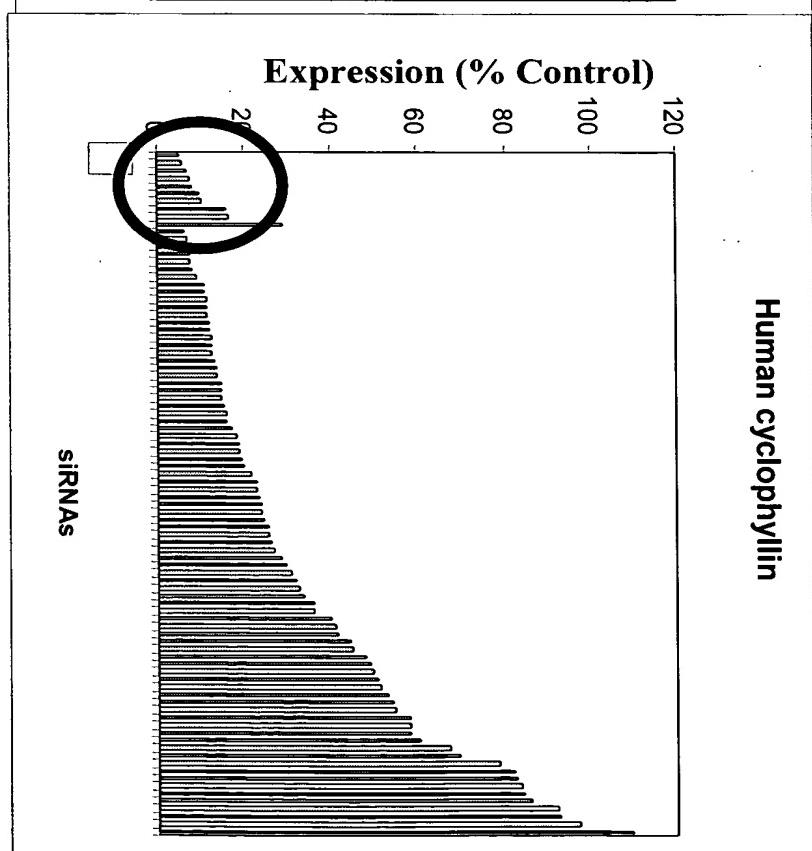


Figure 5B



Differential internal stability

Figure 6a

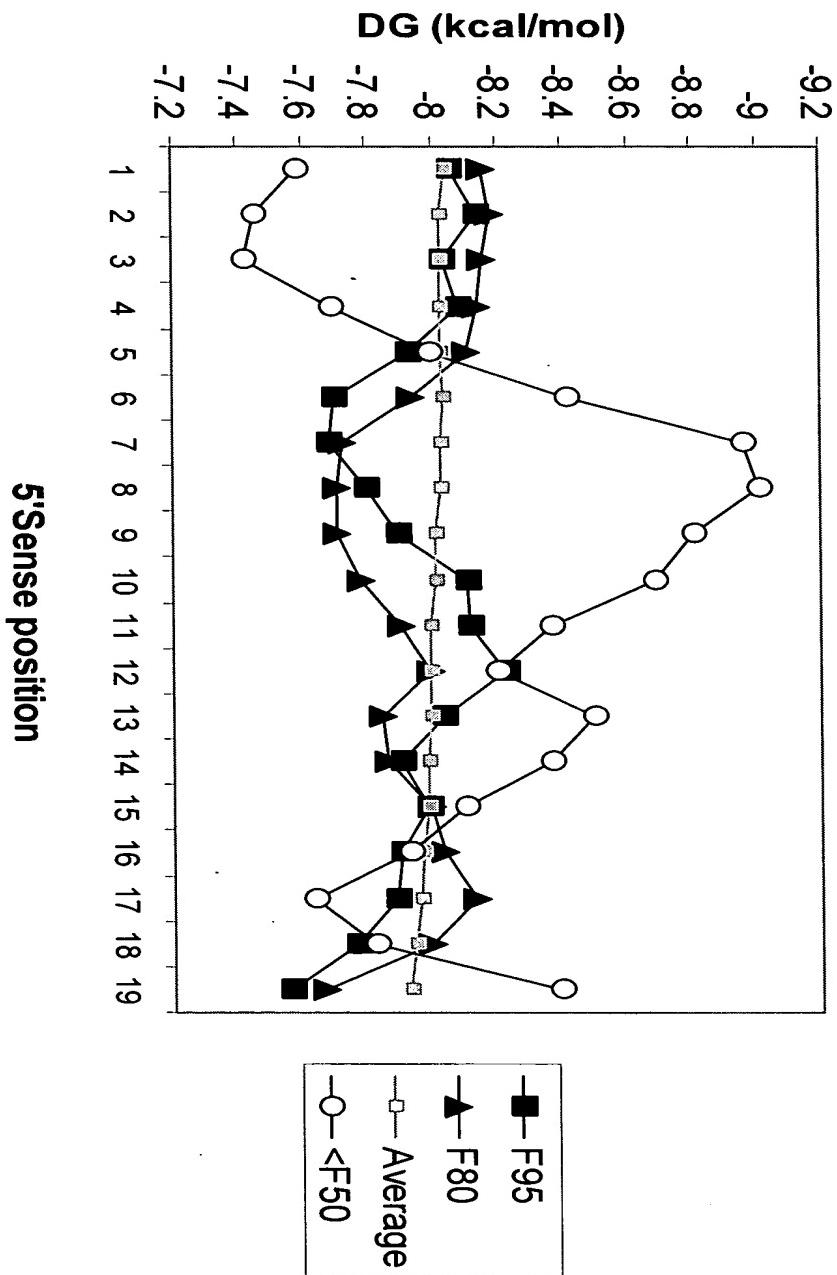


Figure 6b

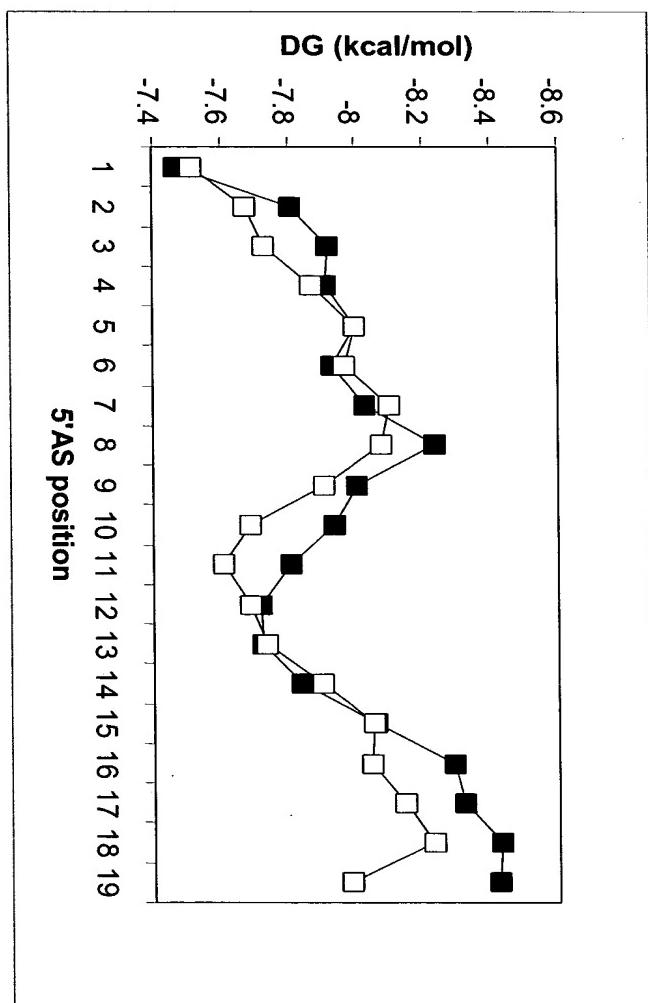
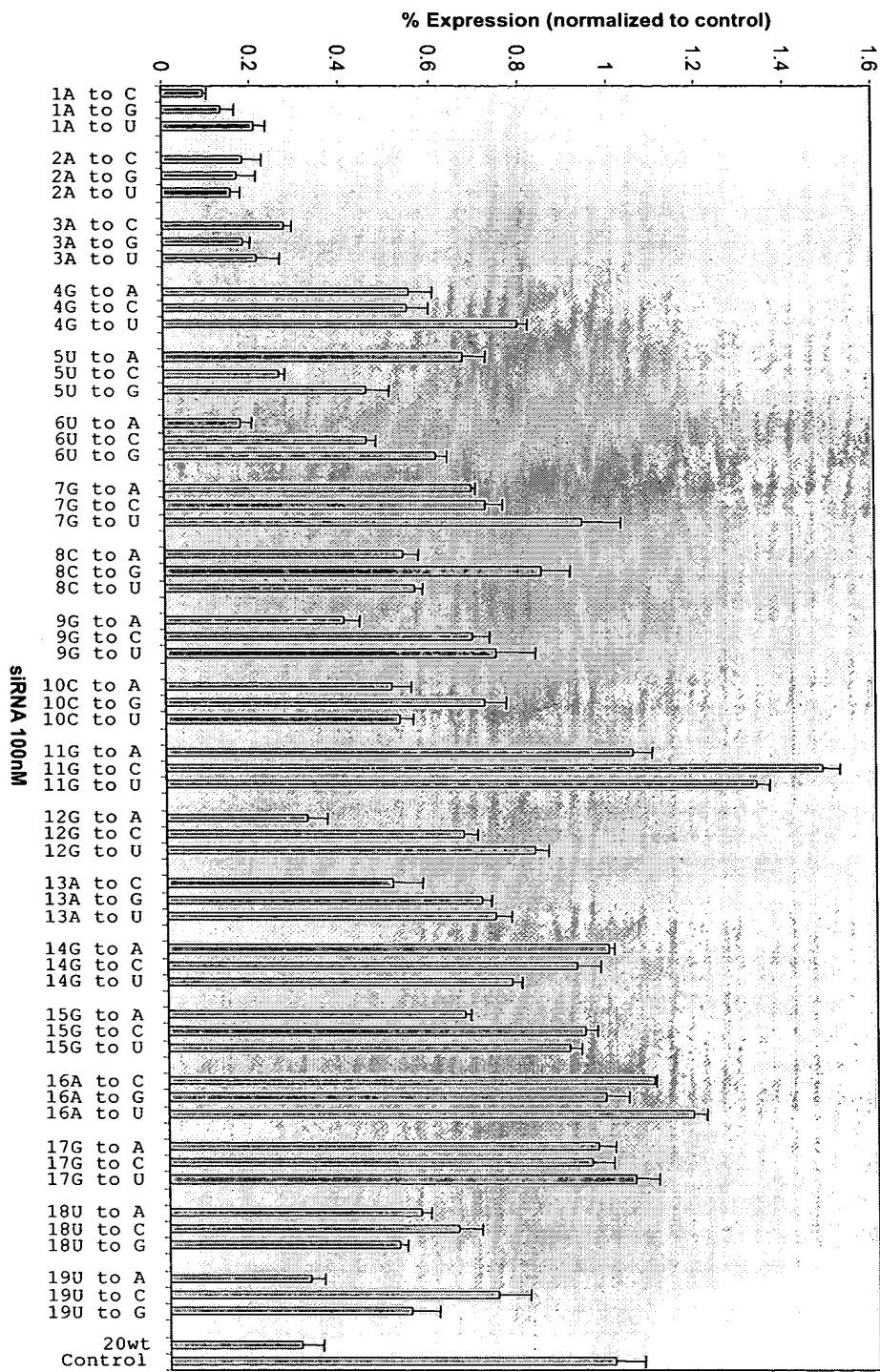
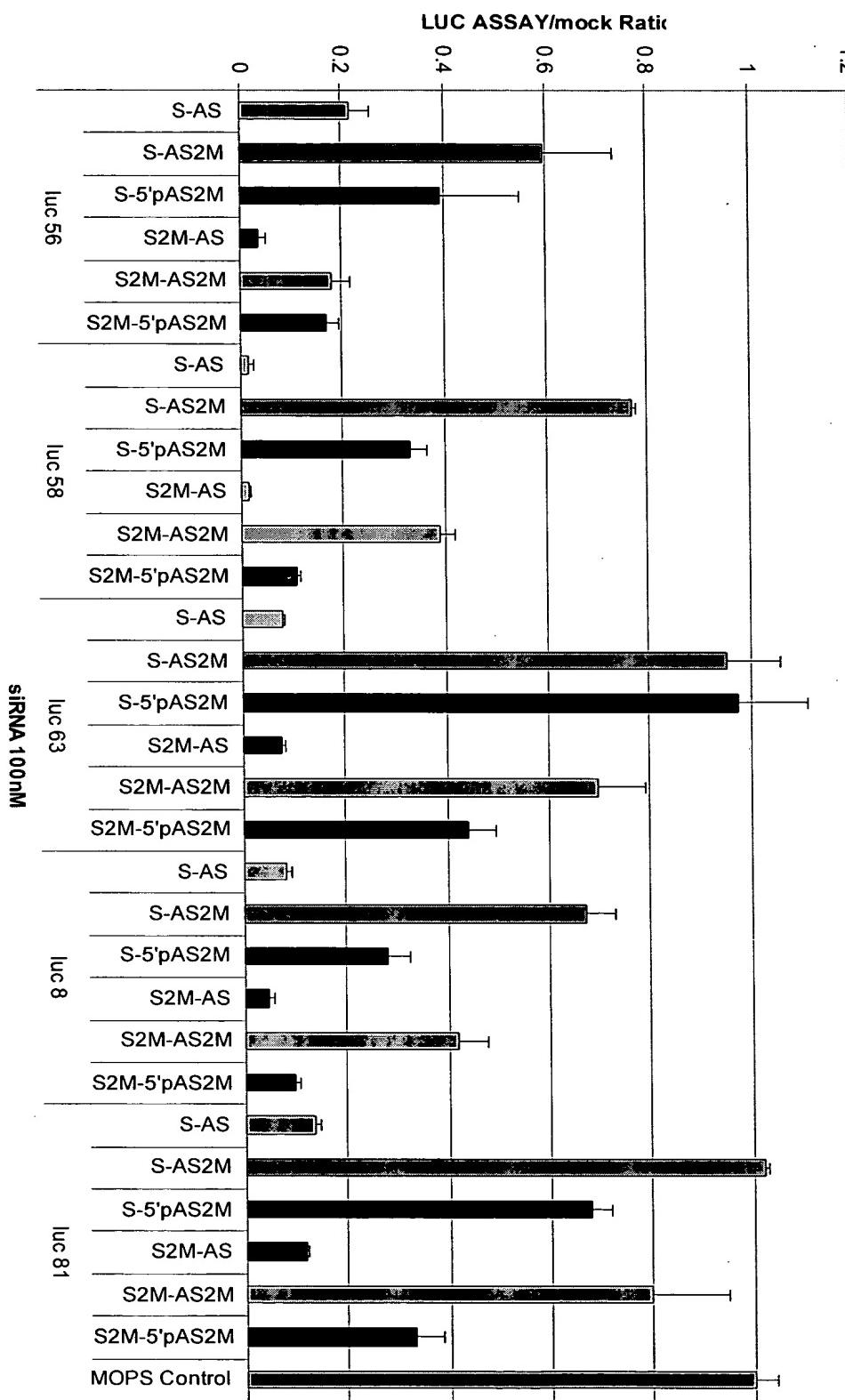


Figure 7



TARGET Screen Normalized LUC ASSAY 293 cells

Figure 8a



CLUSTER ANALYSIS SUMMARY:
Clustered 2363 genes from 6 experiments.
Method = public Scherzer RNAIDharmacon2003 July 2003
Correlation coefficient = 0.91
Correlation p-value = 2.2e-160
Correlation metric type = link
Correlation log base = 2
Correlation p-value = 0.0001
Statistics 193 genes in 6 experiments selected from 2361 genes in 6 experiments

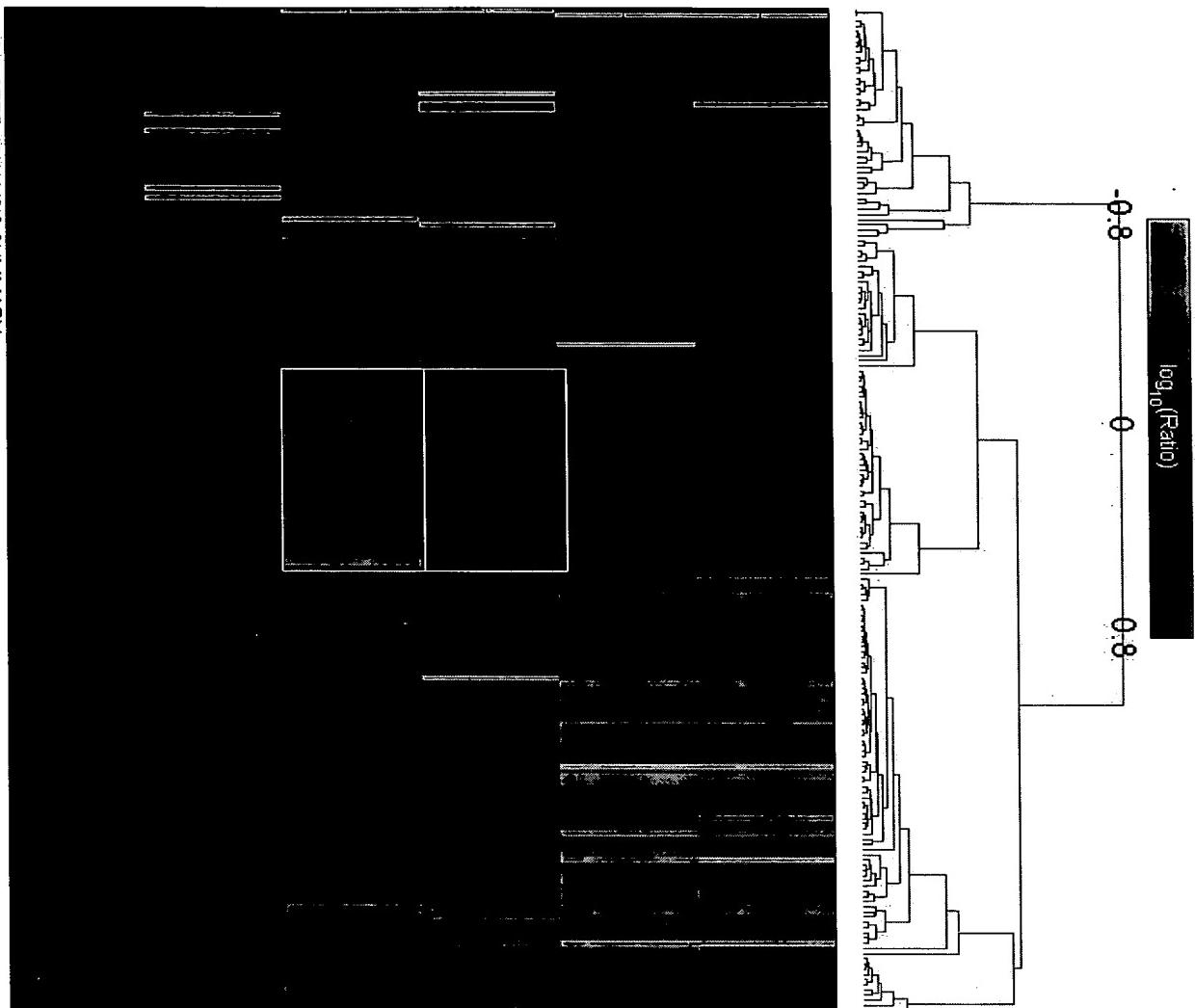


Figure 8b

IGF1R-3
Sense strand modified
IGF1R-3

Figure 9

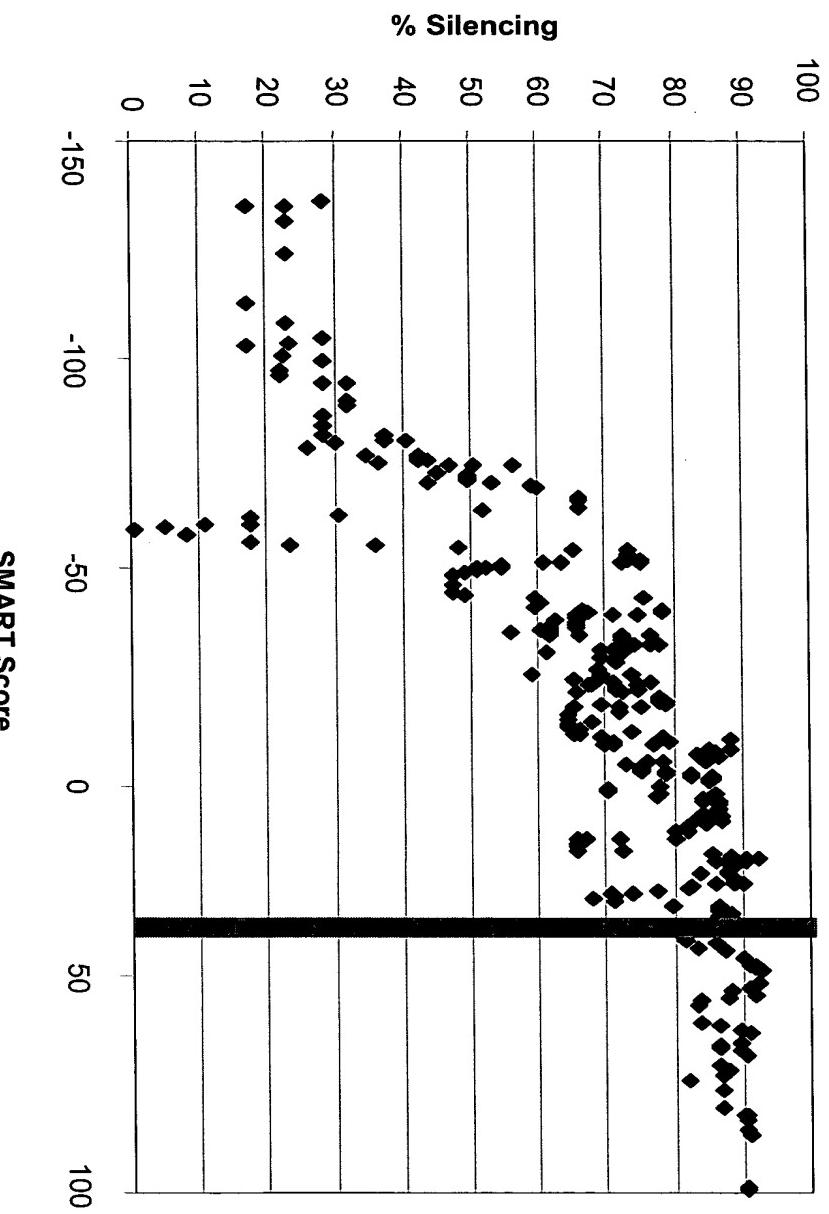


Figure 10a-f

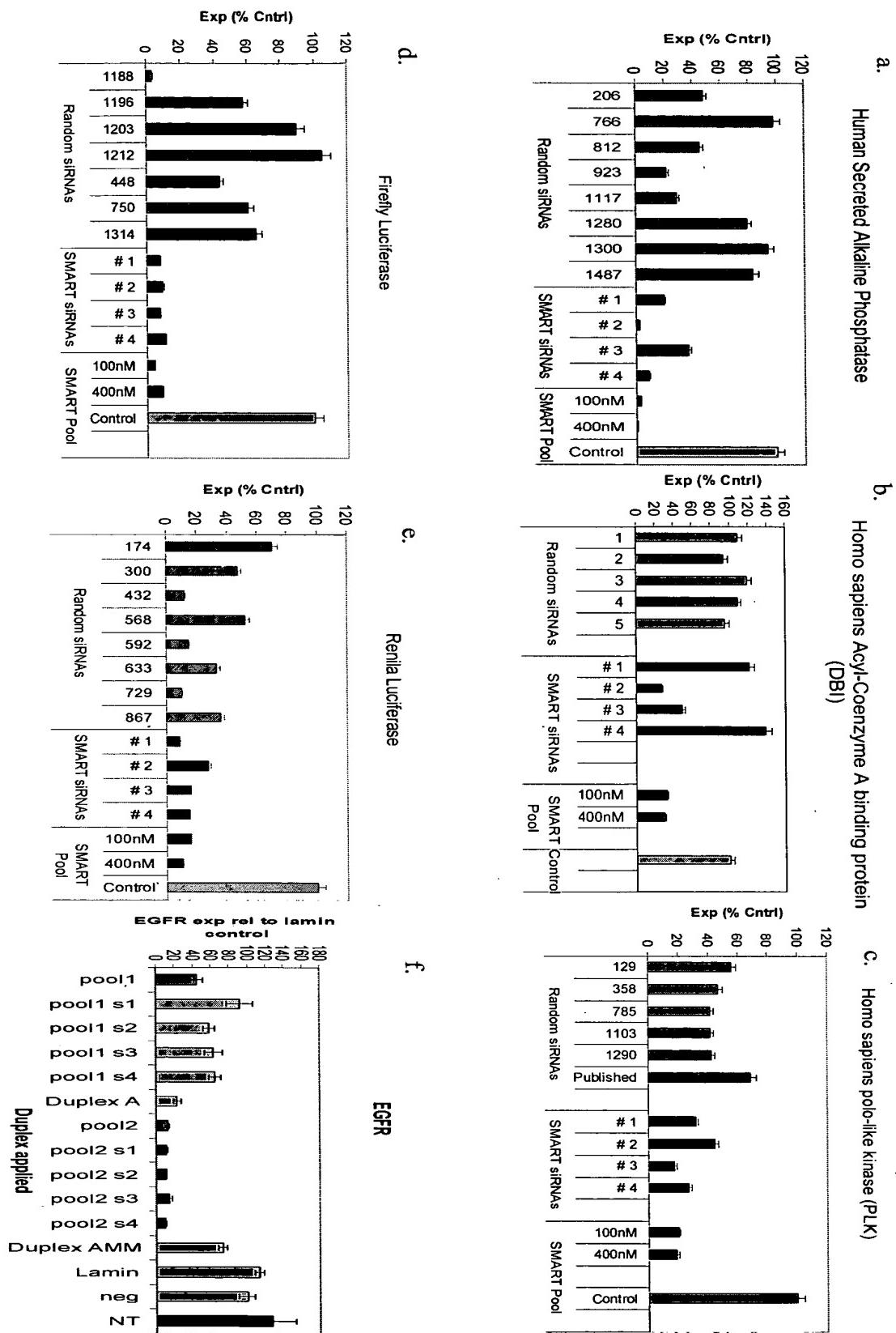
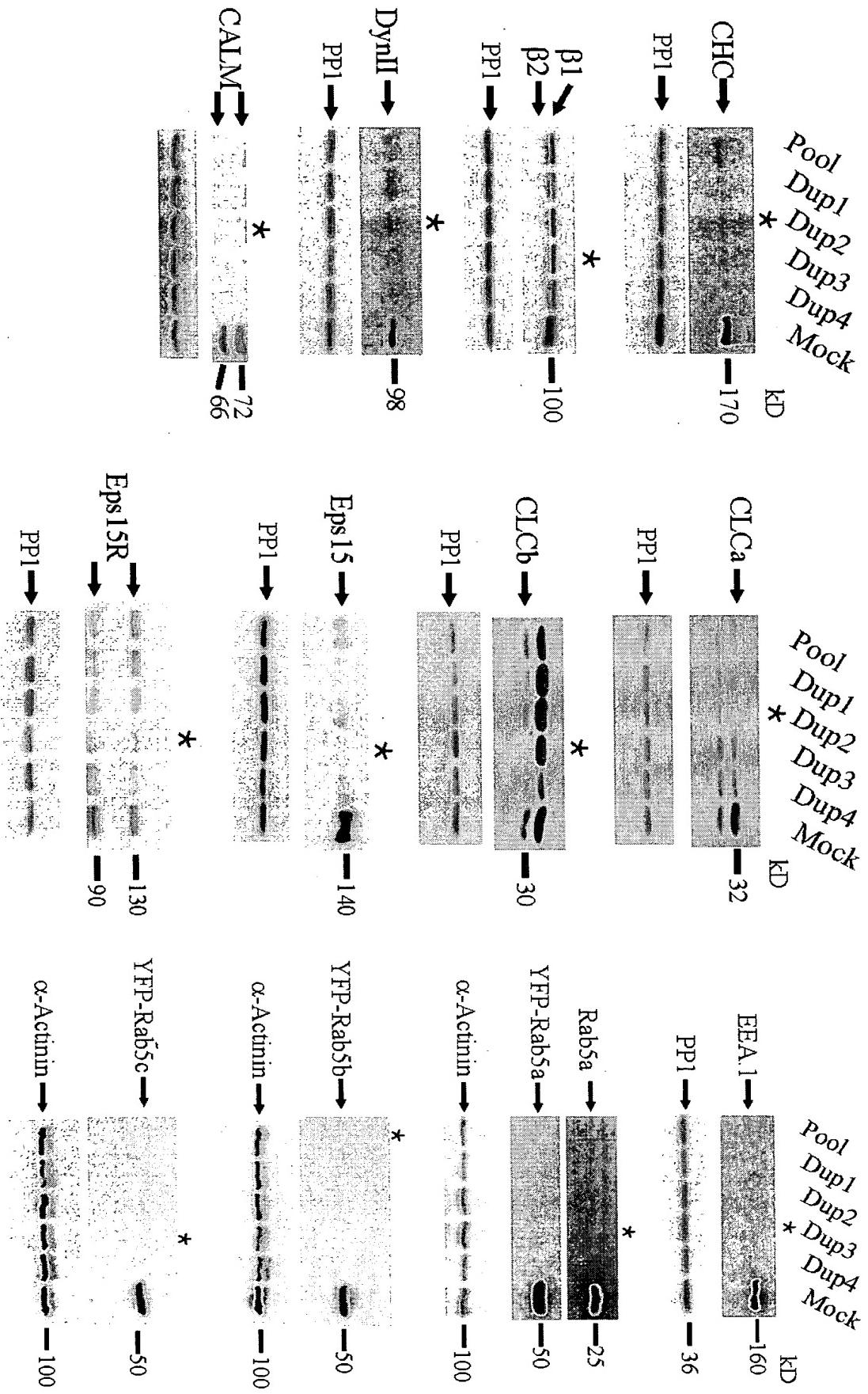


Figure 11



Rational selection validation

Figure 12

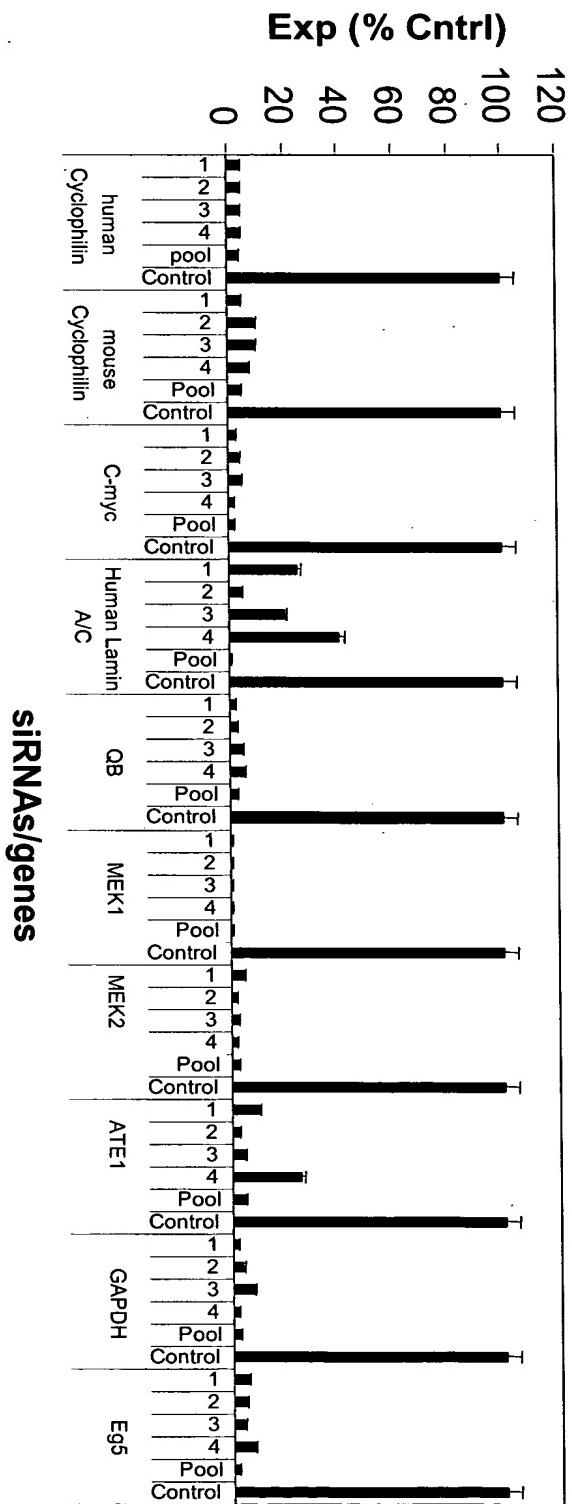
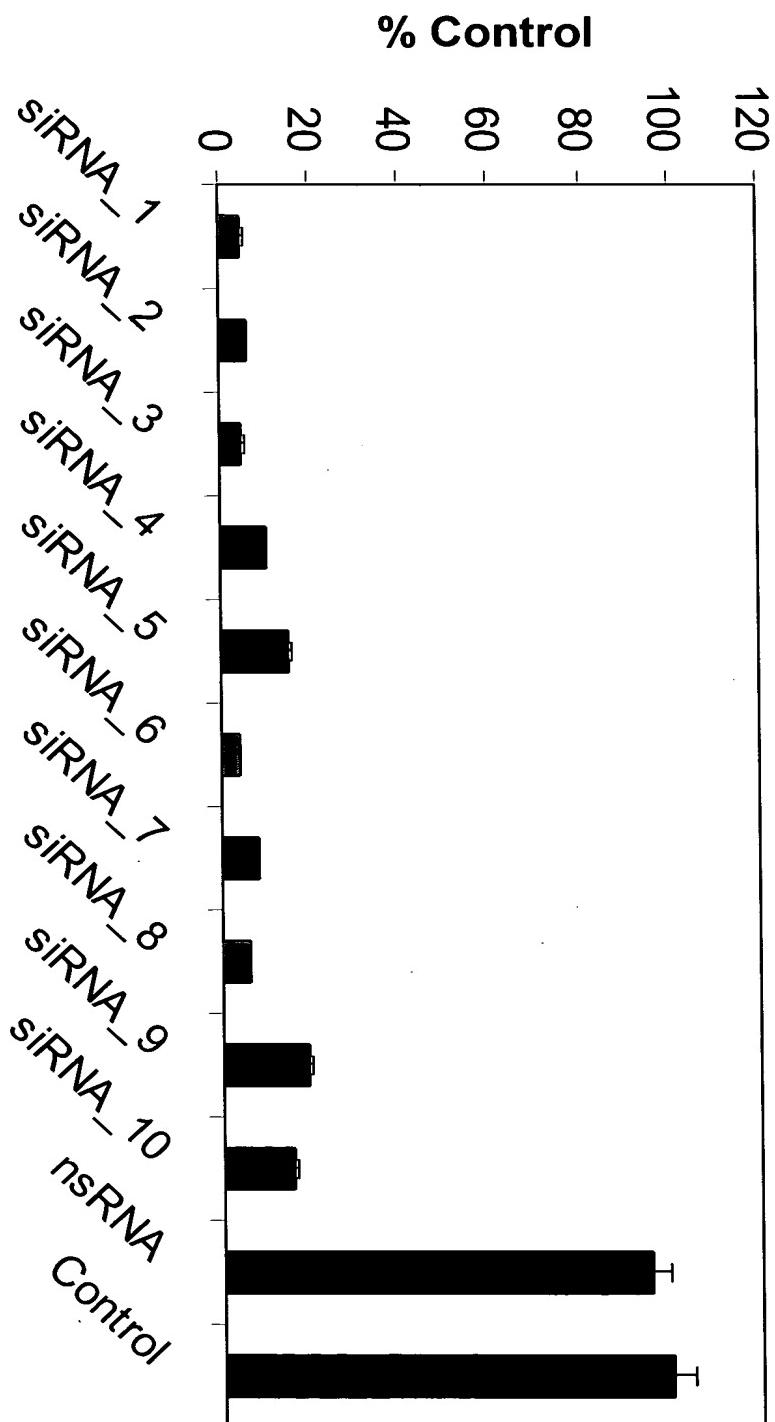


Figure 13 Sequences of top Bcl2

SiRNA 1	GGGAGAUAGUGAUGAAGUA
SiRNA 2	GAAGUACAUCCAUUAAG
SiRNA 3	GUACGACAACGGGAGAUA
SiRNA 4	AGAUAGUGAUGAAGUACAU
SiRNA 5	UGAAGACUCUGCUAGUU
SiRNA 6	GCAUGGCCUCUGUUUGA
SiRNA 7	UGCGGCCUCUGUUUGAUU
SiRNA 8	GAGAUAGUGAUGAAGUACA
SiRNA 9	GGAGAUAGUGAUGAAGUAC
SiRNA 10	GAAGACUCUGCUCAGUUG

**Bcl-2 knockdown by 10 rationally designed siRNAs at
100 nM concentration**

Figure 14



Reporter gene individual siRNAs walk

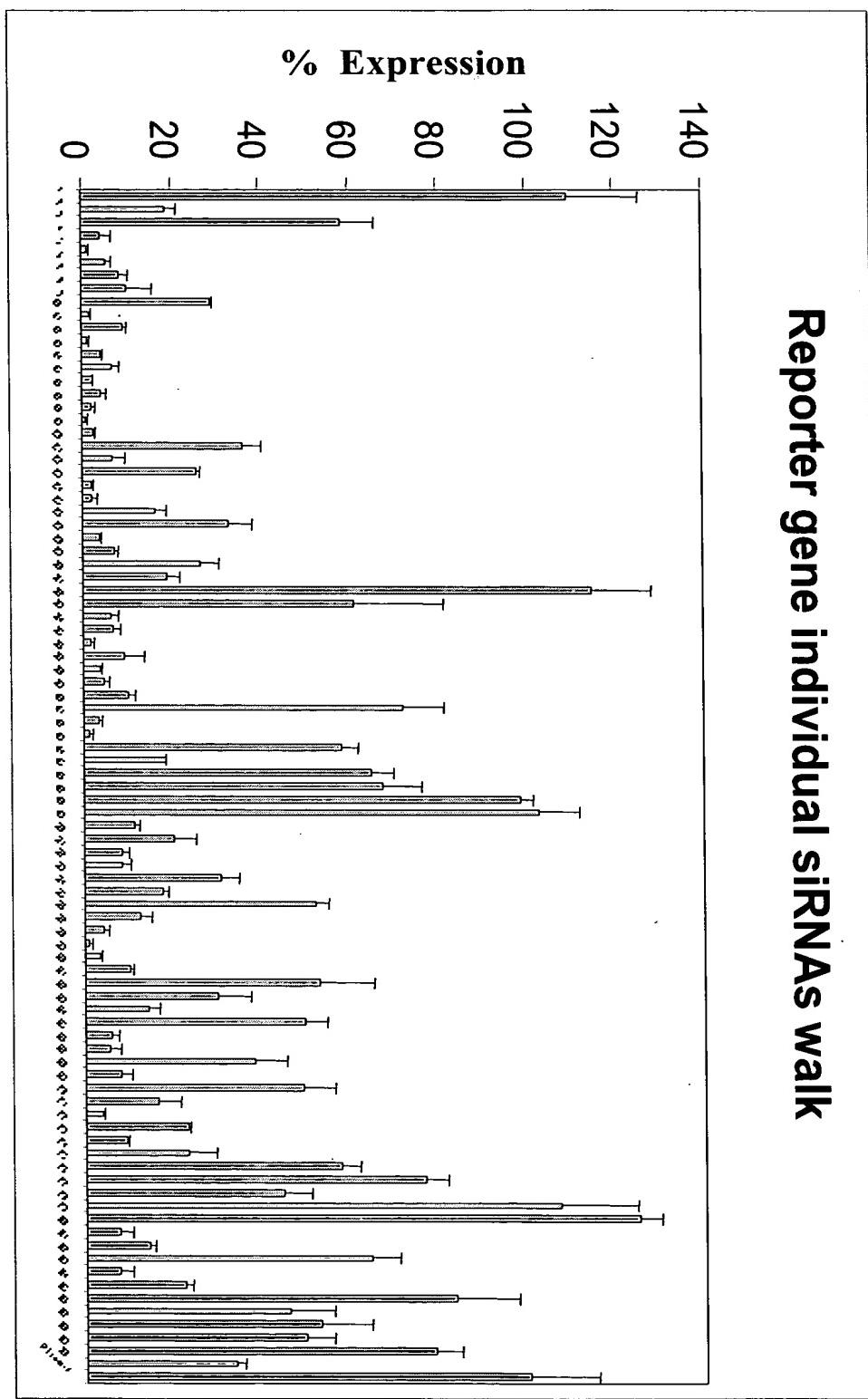
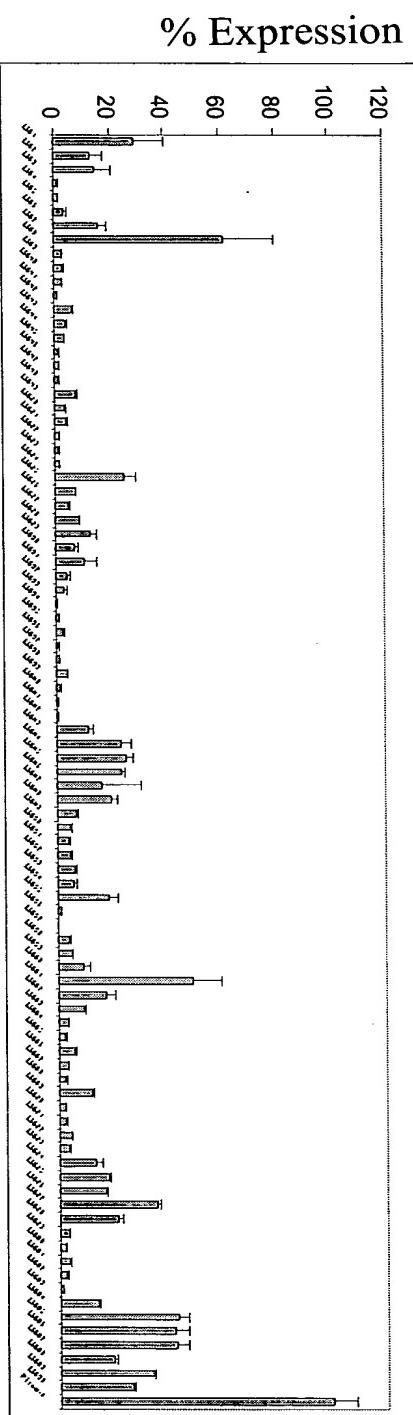
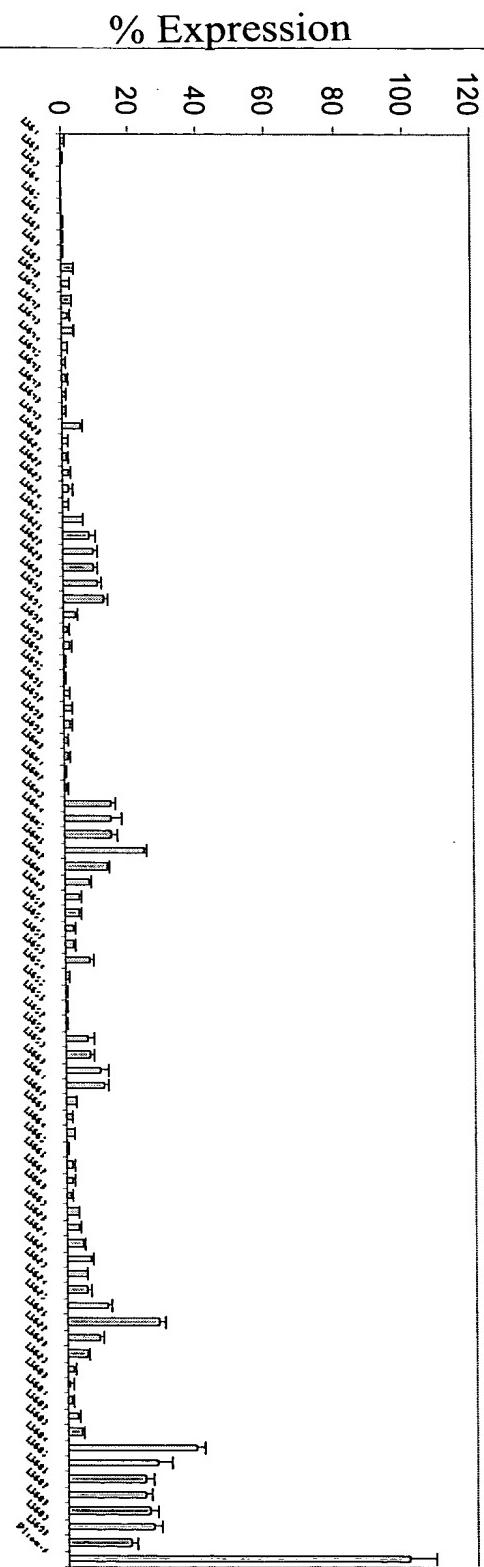


Figure 15

Pools of two walk



Pools of 4 walk



Pools of 5 walk

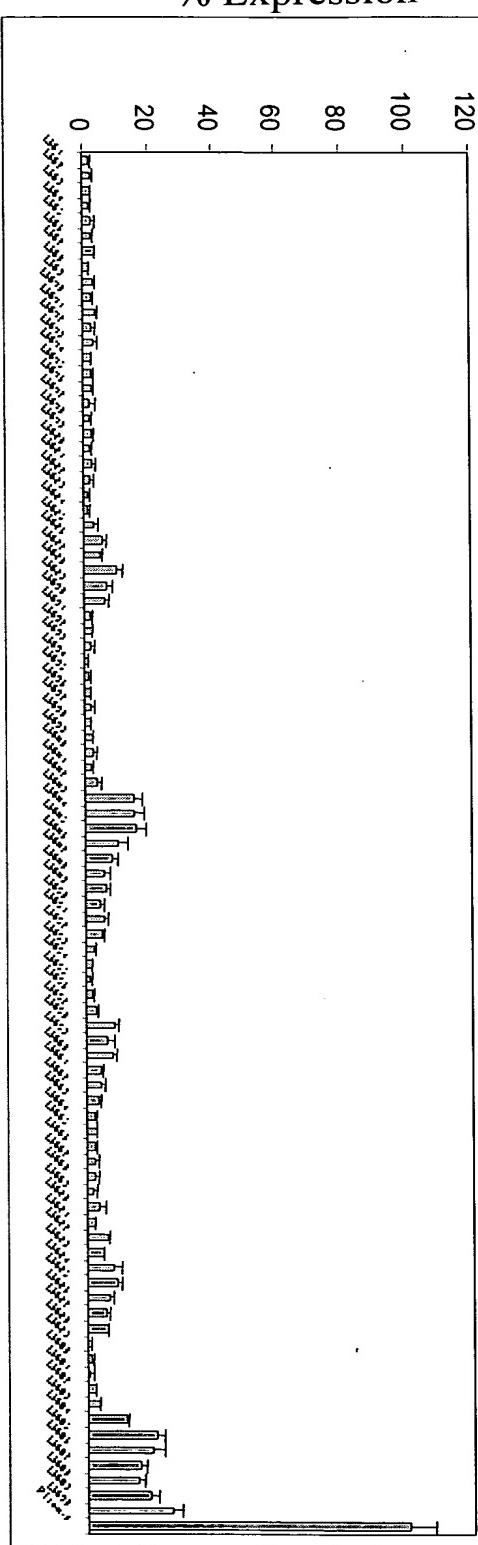


Figure 17

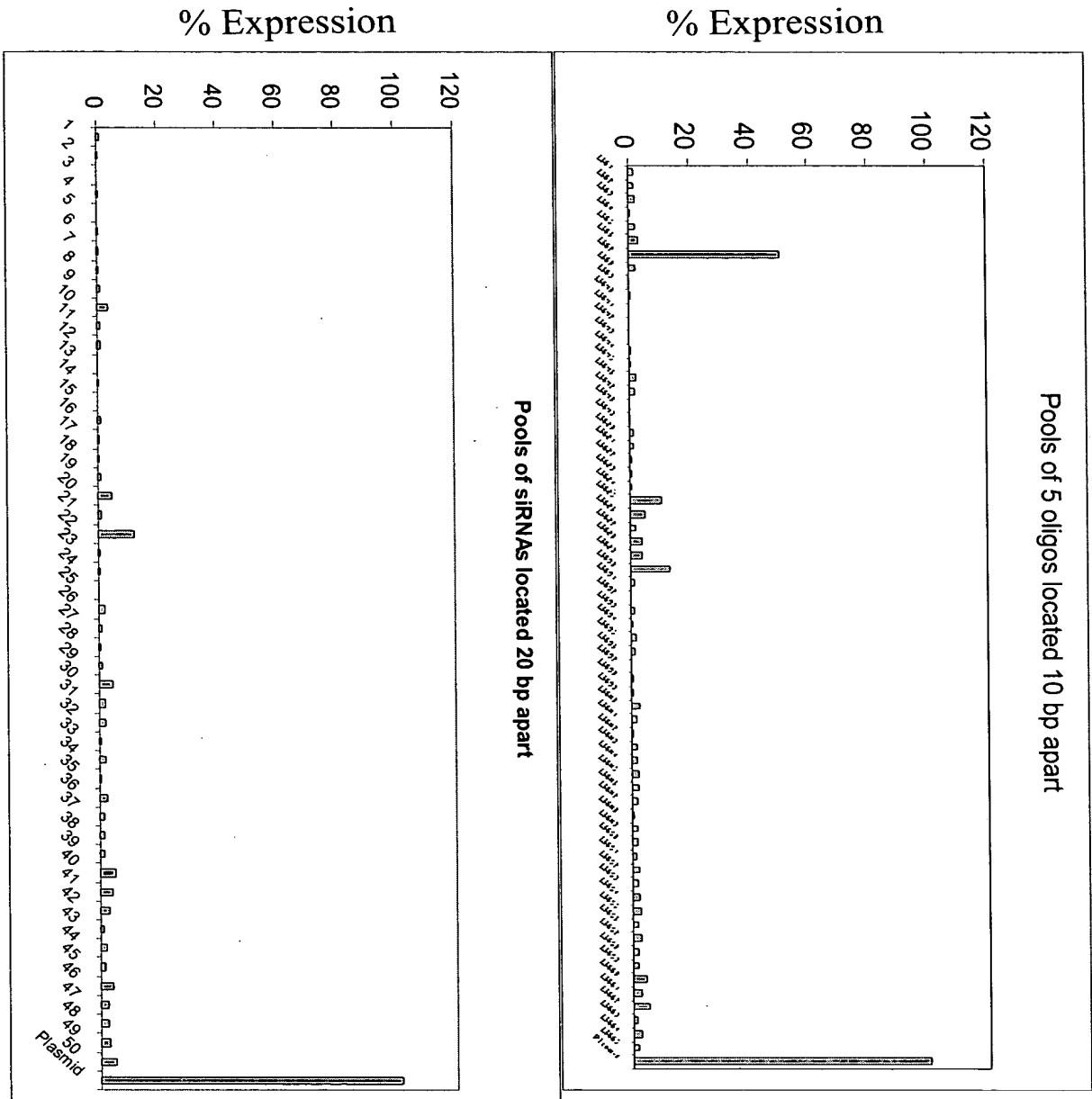
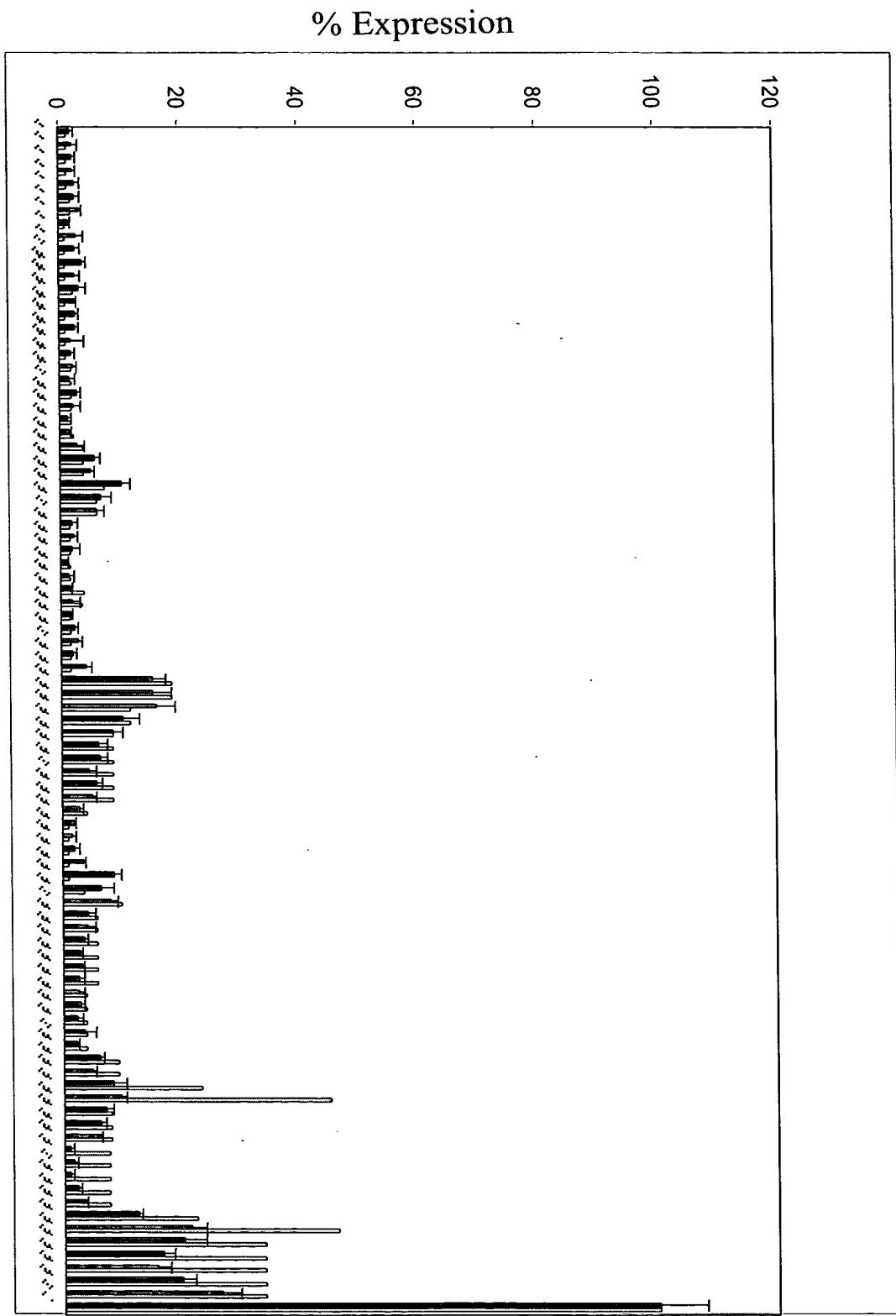


Figure 18

Figure 19



Combination of several semifunctional siRNAs result in a significant improvement of gene expression inhibition

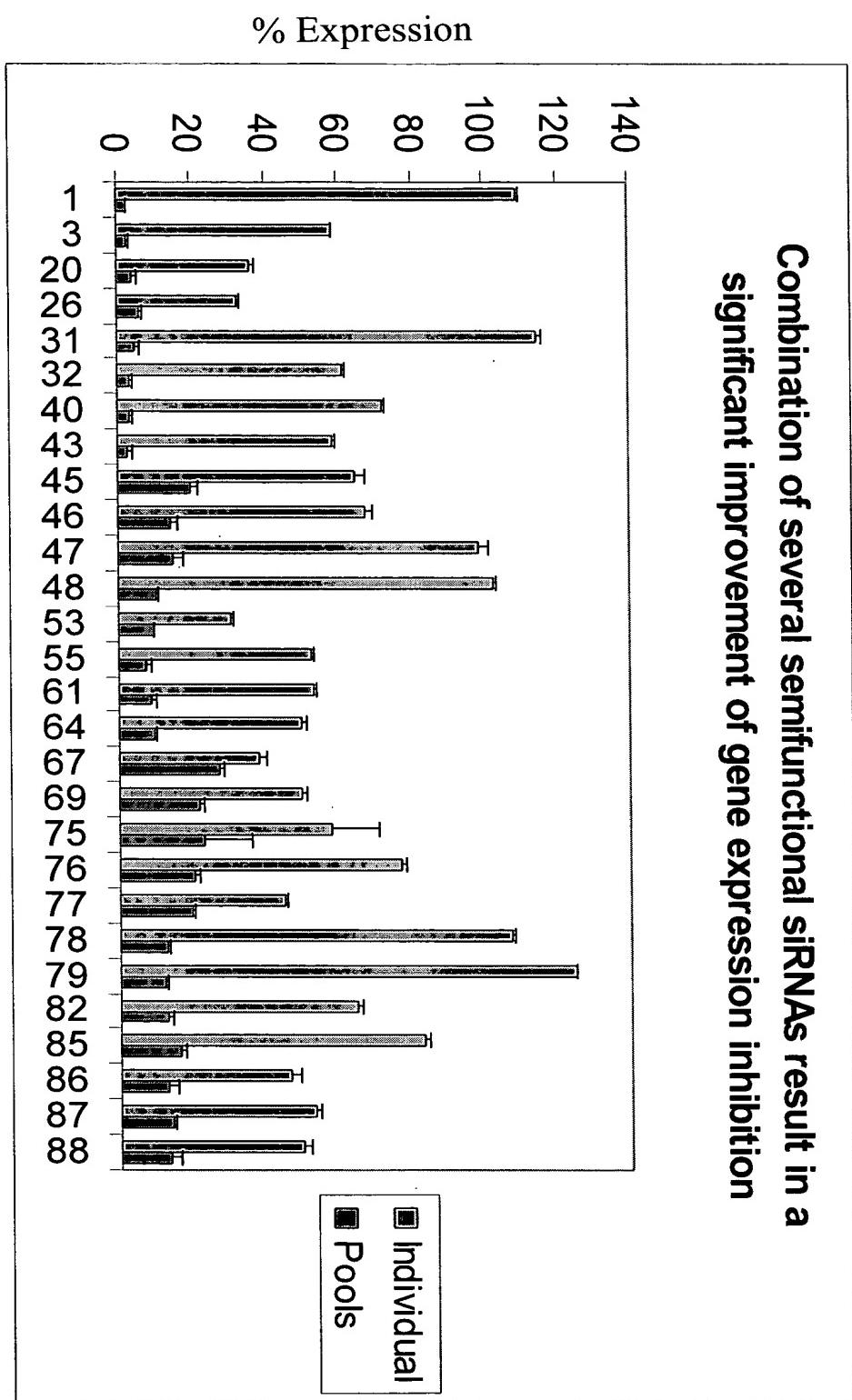


Figure 20

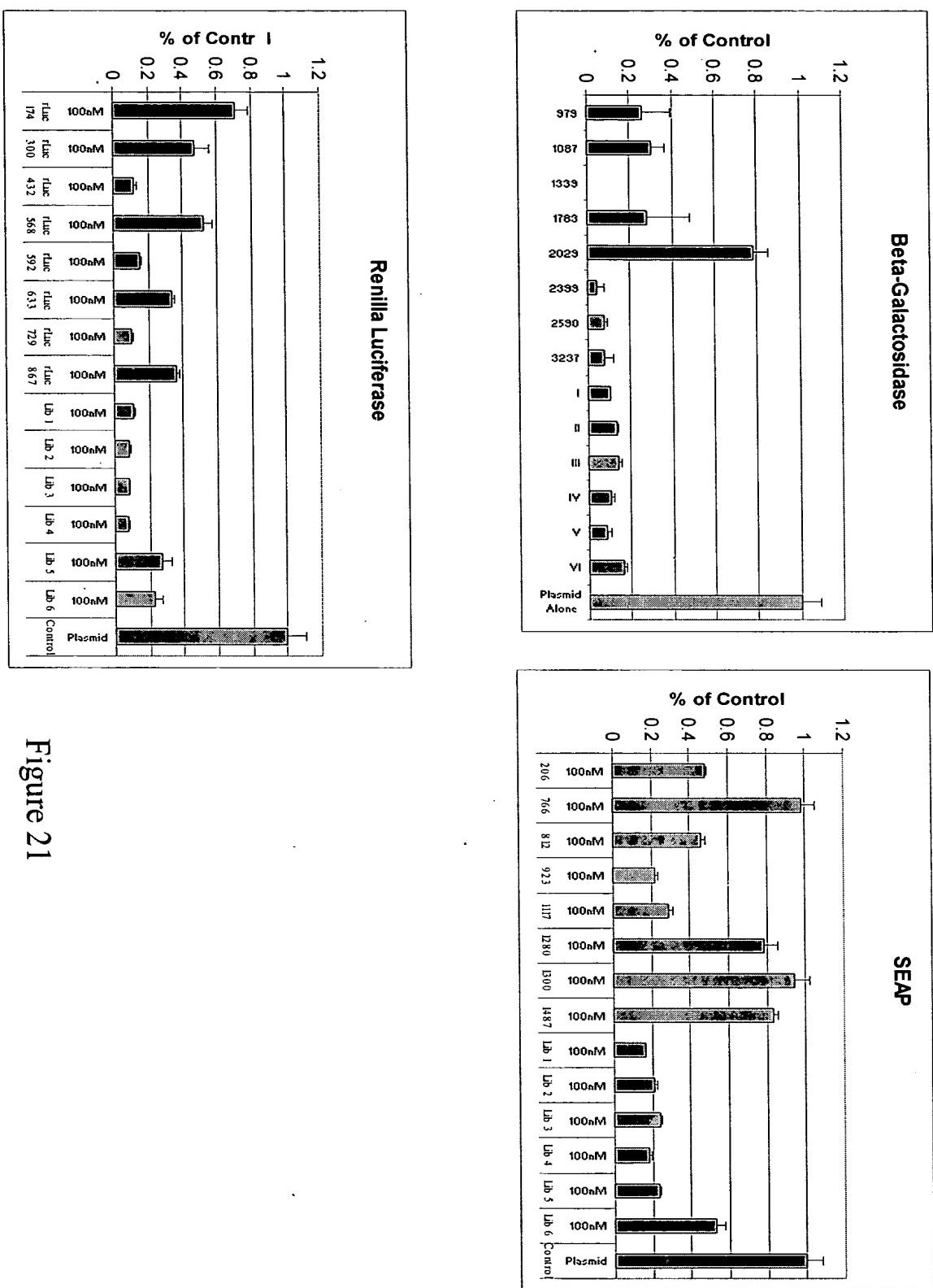


Figure 21

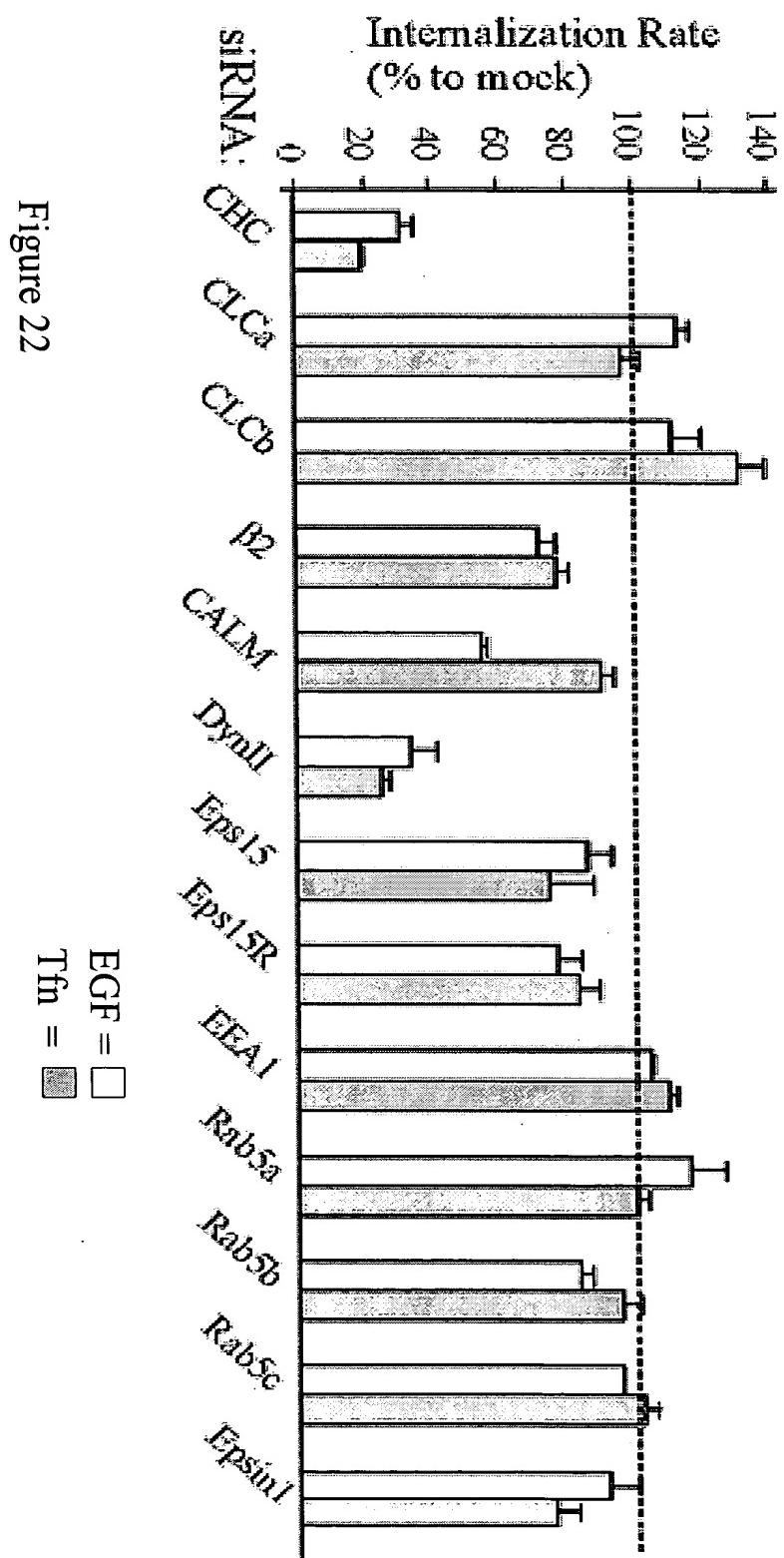


Figure 22

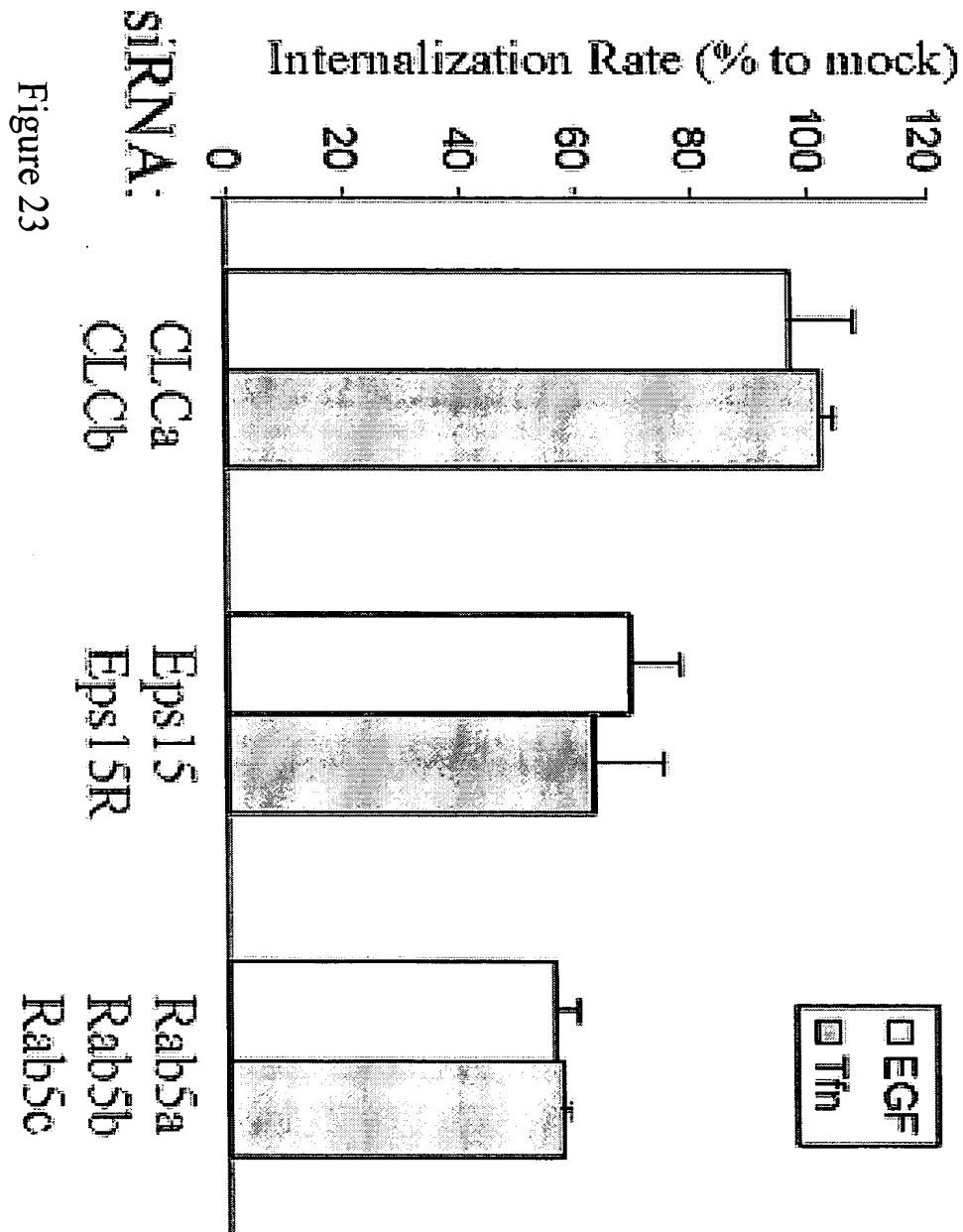


Figure 23

Multitargeting of siRNA

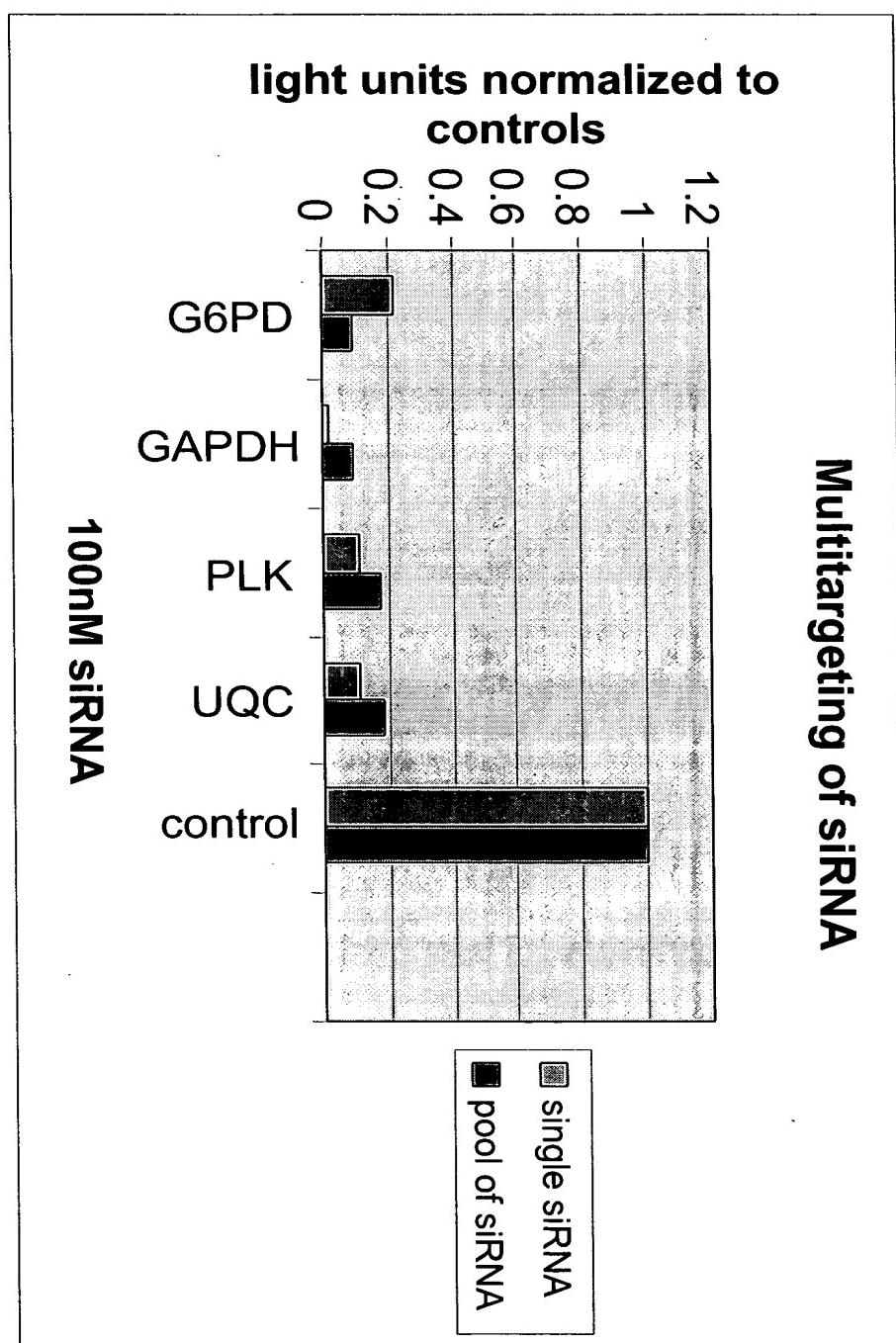


Figure 24

Figure 25

**Bcl-2 knockdown by 10 rationally designed siRNAs at
300 pM concentration**

